

Epidemiology of regional anesthesia in children: Lessons learned from the European Multi-Institutional Study APRICOT

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Abstract

Background: Recently, the European prospective observational multicenter cohort study, APRICOT, reported anesthesia techniques and complications in more than 31 000 pediatric procedures. The main objective of this study was to analyze the current practice in regional anesthesia in the 33 countries that participated to APRICOT.

Methods: Data on regional anesthesia techniques were extracted from the database of APRICOT (261 centers across 33 European countries). All children, aged from birth to 16 years old, were eligible for inclusion during a 2-week period. Type of regional anesthesia, whether used awake or with sedation or general anesthesia, techniques of guidance, and the drugs administered were analyzed.

Results: Regional anesthesia was used in 4377 pediatric surgical procedures. The large majority was performed under general anesthesia with central blocks and truncal blocks, representing, respectively, 42.6% and 41.8% of performed techniques. Caudal blocks represented 76.9% of all central blocks. The penile and ilioinguinal/iliohypogastric blocks were the most commonly performed truncal blocks. Anesthetists used mainly anatomical landmarks; ultrasound guidance was applied in only 23.8% of cases. A wide variability of practices was observed in terms of regional anesthesia techniques and local anesthetics among the participating European countries. No serious complications were reported.

Conclusion: These data show a large predominance of central and truncal blocks in APRICOT study. Ultrasound guidance was mainly used for peripheral nerve blocks while central blocks were performed using landmark techniques.

KEYWORDS

children, Europe, regional anesthesia

1 | INTRODUCTION

During the last decade, a few pediatric cohort studies about pediatric regional anesthesia (RA) were published in the literature. These surveys were mainly focused on some selected institutions¹ or from a given country.² A recent report from the American Pediatric Regional Anesthesia Network (PRAN) confirmed the increasing use and the safety of regional anesthesia in children.³ Interestingly, differences in practice can be noted between the French and the

American reports with an increasing use of peripheral nerve blocks in France in place of caudal blocks. These facts clearly indicate an evolution in the practice of RA in children in comparison with the data published in 1996.⁴

While the increasing use of peripheral nerve blocks (from 38% to 66%) was associated with very rare and minor complications² in the French data, the recent PRAN⁴ report of more than 100 000 blocks from 22 contributing centers in the United States demonstrated a stagnation in the proportion of peripheral nerve blocks around 50%

since 2010.³ In this large series of cases, only transient neurologic deficits were reported with a similar incidence between neuraxial and peripheral blocks.³ Moreover, the generalization of the use of ultrasound guidance to perform peripheral blocks could modify the distribution of the most used regional anesthesia techniques in children.

Recently, the European prospective observational multicenter cohort study, APRICOT, looking at more than 31 000 pediatric procedures did not report any neurologic damage following regional anesthesia.⁵ However, the results show a large variability in the practice of pediatric anesthesia and analgesia in Europe. Therefore, we performed a secondary analysis of the APRICOT study to characterize the epidemiology of regional anesthesia in children across Europe in an attempt to identify areas for potential improvement and harmonization of anesthesia management. The primary outcome was the distribution of the use of central and peripheral blocks. The secondary outcomes were the analysis of the RA guidance techniques and the local anesthetic administered.

2 | MATERIALS AND METHODS

The details of the APRICOT study have already been published previously.⁵ In short, the perioperative data of the children included in the APRICOT study were prospectively collected in 261 participating centers across 33 European countries.⁵ Children were recruited during a consecutive 2-week period; freely chosen by the participating centers, between April 1, 2014, and January 31, 2015. The APRICOT study was registered with ClinicalTrials.gov (number NCT01878760). Patients were followed for up to 60 minutes after anesthesia or sedation. All children up to 16 years old undergoing an inpatient or outpatient diagnostic or surgical procedure, under sedation or general anesthesia, with or without regional anesthesia, were eligible for inclusion in APRICOT study.⁵ The complete registration form was filled in by the anesthesia team in charge of the patients, and the data collected were related to the anesthesia management itself. For the current analysis, we extracted all surgical procedures as they are the only to be associated with RA.

In each APRICOT case report form, a specific item was dedicated to the performance of RA. If RA was performed, a specific supplementary questionnaire had to be completed. In addition to demographic data, surgical indication, personal, and familial history, we recorded the type of RA, the association or not with sedation or general anesthesia, technique of guidance of RA (landmarks, nerve stimulation, ultrasound, association of both), and the local anesthetic and adjuvant administered in RA. Patients were classified in 6 age groups: less than 1 month, 1 to <6 months, 6 to <12 months, 1 to <3 years, 3 to <12 years, and 12 to 15 years old.

We also collected data on the number and type of RA blocks performed in each country during the study period. Finally, the use of ultrasound guidance and the type of local anesthetic used for each country were also analyzed.

What is already known

- Regional analgesia has proven useful in improving the treatment of postoperative pain and reducing the use of systemic analgesics such as opioids.
- Several studies have demonstrated the low incidence of complications associated with peripheral blocks.

What this article adds

- The low frequency of regional analgesia in pediatric anesthesia practice in Europe.
- Central blocks remain extremely popular in Europe and seem to be favored by peripheral blocks for some countries.

2.1 | Statistical analysis

The study size for APRICOT was based on the estimation of severe critical events of general anesthesia or sedation, not regional anesthesia. The current secondary analysis is focused on the use of regional analgesia in the centers that participated to APRICOT. APRICOT study is purely an observational study. Thus, descriptive data are expressed as median (interquartile ratio) for continuous variables and numbers (percent) for categorical variables. Statistical analysis was performed using SAS enterprise guide version 7.1 (SAS Institute). The study was registered with ClinicalTrials.gov, number NCT01878760.

3 | RESULTS

Out of 31 127 procedures included in APRICOT study, we extracted 22 224 surgical procedures. Regional anesthesia was reported in 6900 of these surgical procedures performed on 6892 children, representing a rate of 31%. Four hundred and nineteen RA procedures (7.2%) were noted as "others" without any other precision and were excluded from analysis. We decided also to exclude surgical infiltration ($n = 2106$) because we have no precision on "who", "how", and "for which indication" these RA were performed. The final analysis therefore included a total of 4377 peripheral or central blocks. Rates of RA use during the study period in the different participating centers of each country are represented in Figure 1.

The median age was 4.9 (1.6-9.3) years. Table 1 summarizes the distribution of the different RA procedures according to age. RA was more frequently performed in children aged 3 to 11 years. The number of RA according to age range is presented in Figure 2. 78.6% of children were boys and 72% of children undergoing regional anesthesia were scored ASA physical status I, 22% ASA II, 5% I ASA III, and 1% ASA IV. Most of the RA were used during elective surgery ($n = 3650$, 83.4%).

The large majority of the RA was performed under general anesthesia ($n = 4005$, 94.3%). The practice of RA in awake children

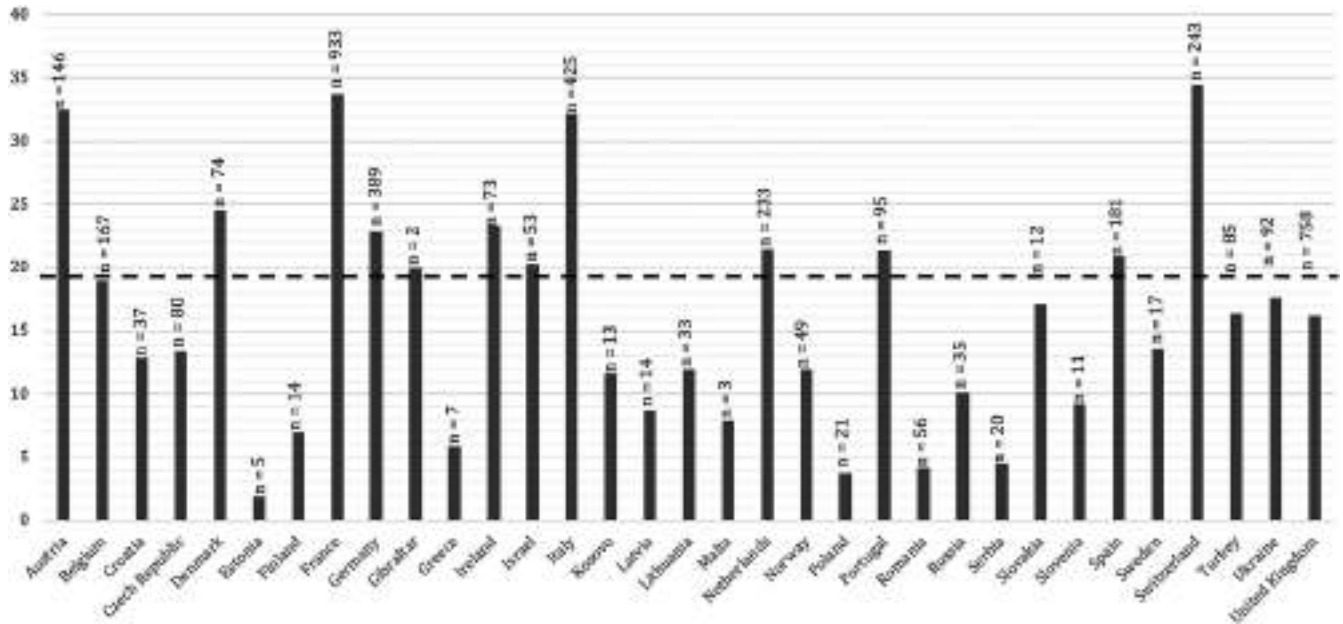


FIGURE 1 Percentage of regional anesthesia (without others and infiltrations) per country (n = 4377). (Dashed line represents the percentage value of regional anesthesia without others and infiltrations among all countries in Europe)

TABLE 1 Distribution of regional anesthesia techniques for surgical procedures according to patients' age. (Single data are presented as absolute value and the total number as percentage)

Techniques	<1 mo	1 to <6 mo	6 to <12 mo	1 to <3 y	3 to <12 y	>12 y	Total blocks	%
Central								
Spinals	8	33	4	3	22	45	115	6.2
Caudals	43	236	123	481	518	34	1435	76.9
Lumbar EB	1	6	10	26	108	59	210	11.3
Thoracic EB	2	6	10	14	28	43	105	5.6
Sub-Total 1	54 (2.9%)	283 (15.2%)	147 (7.9%)	524 (28.1%)	676 (36.2%)	181 (9.7%)	1865	100
Truncal								
II-IH blocks	0	34	20	121	294	45	514	28.1
TAP blocks	9	14	7	37	158	49	274	15
Intercostal	1	3	1	0	6	2	13	0.7
Paraumbilical	9	10	1	12	66	7	105	5.8
Penile	2	15	22	154	503	103	799	43.6
Pudendal	0	0	10	34	68	13	125	6.8
Sub-Total 2	21 (1.1%)	76 (4.2%)	61 (3.3%)	358 (19.6%)	1095 (59.8%)	219 (12%)	1830	100
Upper limb	0	0	5	41	141	72	259	
Lower limb	0	1	3	15	121	172	312	
Craniofacial	4	20	11	19	36	21	111	
Total	79 (1.8%)	380 (8.7%)	227 (5.2%)	957 (21.9%)	2069 (47.2%)	665 (15.2%)	4377	

Abbreviations: EB, epidural blocks; II-IH, ilioinguinal-iliohypogastric; Paraumb, paraumbilical; TAP, trans-abdominis plane.

was rare (n = 61, 1.4%) and 189 (4.3%) procedures were performed under sedation. Among the patients undergoing awake RA, almost two third (n = 49, 80%) were younger than 6 months of age and all of them underwent spinal or caudal anesthesia. The 12 other children who had a RA while awake were aged from 1 to 3 years old and underwent 10 upper limb blocks and 2 lower limb blocks.

3.1 | Epidemiology

Analyzing the RA techniques reveals that central blocks (42.6%) and truncal blocks (41.8%) were the most commonly performed followed by lower limb blocks (7.1%), upper limb blocks (5.9%), and craniofacial blocks (2.6%). Caudal blocks represented 76.9% of all central blocks,

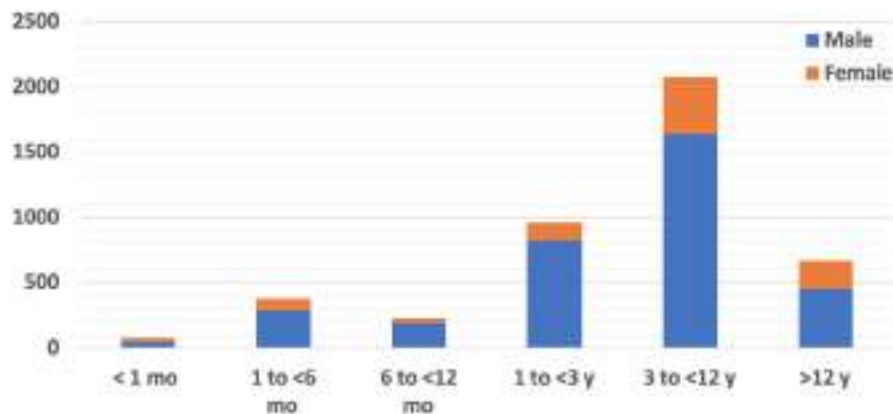


FIGURE 2 Age range and sex distribution of the 4377 regional anesthetic procedures reported in APRICOT database (except "other" and "infiltrations")

and more than 87% were performed in children up to 3 years. Spinal anesthesia, thoracic epidural, and lumbar epidural represented 6.2%, 5.6%, and 11.3% of all central blocks, respectively (Table 1). The central block was associated with another RA techniques in 2.5% of cases and peripheral nerve blocks in 10.8% of them. Pudendal block was the most commonly performed block in association with others blocks (61%), usually trans-abdominis plane block or ilioinguinal/iliohypogastric block. Moreover, the trans-abdominis plane block and the ilioinguinal/iliohypogastric blocks were associated with others blocks in 14.6% and 21.2% of cases, respectively.

Among truncal blocks, penile block and ilioinguinal-iliohypogastric block were the most commonly performed. More than 90% of truncal blocks were performed in children between 1 and 16 years old. Table 1 summarizes the distribution of the different truncal blocks according to children's age.

The distribution of the central, caudal, and truncal blocks per country is reported in Table 2.

3.2 | Technical aids for RA

The majority of RA was performed using anatomical landmarks (72.6%). Ultrasound guidance was used in 23.8% of all cases (alone in 20.2% and in association with nerve stimulation in 3.6%). The use of ultrasound guidance varied widely among the countries (Figure 3).

Ultrasound guidance associated or not with nerve stimulation was used in 66% of upper limb blocks and 70% of lower limb blocks (Table 3). Nerve stimulation was used alone in only 3.6% of cases, among which nearly 50% of pudendal blocks. Most of central blocks (97%) and craniofacial blocks (89%) were performed with landmarks techniques. For truncal blocks, a majority of TAP blocks (96%) were performed with ultrasound guidance. Details of localizing aid technical for truncal blocks are given in Table 3.

3.3 | Local anesthetic for RA

Levobupivacaine and ropivacaine were the most frequently used LA: in 37.6% and 37.1% of patients, respectively. Bupivacaine, lidocaine, and prilocaïne were administered in 24.2%, 1.1%, and 0.1% of cases, respectively. The distribution of the use of different LA-types

is quite comparable between bupivacaine, levobupivacaine, and ropivacaine with, respectively, 25%, 34%, and 41% in central blocks and 23%, 40%, and 34% in peripheral blocks. Another LA, such as mepivacaine, articaine, trimecaine, and tetracaine, were rarely used.

Clonidine was the most frequently used adjuvant in 400 children (9.1%) and was associated with ropivacaine ($n = 193$), levobupivacaine ($n = 142$), or bupivacaine ($n = 65$). Many other adjuvants (such as an opiate, dexamethasone, bicarbonate, or ketamine) were reported anecdotally.

3.4 | Complications

Only one side effect was noted in the whole study. It was an error of side during the performance of regional anesthesia. No case of systemic toxicity, long-term complication or death was reported.

4 | DISCUSSION

The present study provides valuable information on the current RA practice in 2015-2016 in 261 participating centers among 33 European countries. The results revealed that RA was used in a third of all surgical procedures, and peripheral limb nerve blocks represented only 19.6% of all RA. In our study, central blocks and truncal blocks were the most frequently performed. However, an age-dependent RA variation of practice could be identified with a majority of truncal blocks being more often considered in children older than 3 years while central blocks and primarily caudal blocks being performed in children aged 3 and less. This study revealed that European anesthetists have usually access to ultrasound for their guidance for RA to perform a truncal block. Finally, there were no reports of neurologic damage or anesthetic toxicity.

The current study offers an opportunity to evaluate practice patterns in European countries. The rate of RA use is comparable to the last reports from the ADARPEF in France.² Moreover, and similarly to what is reported in the literature, the vast majority of the blocks were performed under general anesthesia or sedation.^{1,2} One main finding in the present study is that peripheral nerve blocks (trunk, upper and lower limb, and craniofacial) are now

TABLE 2 Distribution of central blocks, caudal blocks, and truncal blocks per country. Expressed in number (%)

Country	Central Blocks	Caudal blocks	Truncal blocks
Austria	91 (62.3)	81 (55.5)	45 (30.8)
Belgium	62 (37.1)	42 (25.1)	93 (55.7)
Croatia	4 (10.8)	0	29 (78.4)
Czech Republic	70 (87.5)	63 (78.8)	0
Denmark	24 (32.4)	15 (20.3)	26 (35.1)
Estonia	5 (100)	1 (20)	0
Finland	7 (50)	6 (42.9)	7 (50)
France	204 (21.9)	116 (12.4)	533 (57.1)
Germany	276 (71)	263 (67.6)	71 (18.3)
Gibraltar	0	0	2 (100)
Greece	0	0	7 (100)
Ireland	21 (28.8)	16 (21.9)	30 (41.1)
Israel	23 (43.4)	16 (30.9)	25 (47.2)
Italy	166 (39.1)	116 (27.3)	215 (50.6)
Kosovo	11 (84.6)	11 (84.6)	2 (15.4)
Latvia	13 (92.9)	5 (35.7)	0
Lithuania	16 (48.5)	15 (45.5)	8 (24.2)
Malta	1 (33.3)	1 (33.3)	2 (66.7)
Netherlands	160 (68.7)	120 (51.5)	44 (18.9)
Norway	28 (57.1)	22 (44.9)	8 (16.3)
Poland	16 (76.2)	7 (33.3)	5 (23.8)
Portugal	38 (40)	28 (29.5)	48 (50.5)
Romania	21 (37.5)	6 (10.7)	30 (53.6)
Russia	20 (57.1)	10 (28.6)	13 (36.1)
Serbia	6 (30)	5 (25)	8 (40)
Slovakia	9 (75)	9 (75)	3 (25)
Slovenia	8 (72.7)	7 (63.6)	3 (27.3)
Spain	33 (18.2)	21 (11.6)	130 (71.8)
Sweden	3 (17.6)	2 (11.8)	14 (82.4)
Switzerland	115 (47.3)	105 (43.2)	81 (33.3)
Turkey	19 (22.4)	17 (20)	66 (77.6)
Ukraine	44 (47.8)	28 (30.4)	3 (3.3)
United Kingdom	351 (46.3)	281 (37.1)	278 (36.7)

Note: Expressed in number and percentage of the central blocks, caudal blocks, or truncal blocks calculated in relation to the total number of RA without "others and infiltrations" declared in each country (n = 4377).

more frequently performed than central blocks. This trend may be explained by the reports from ADARPEF and PRAN studies that underlined the safety of peripheral nerve blocks compared with central blocks and encouraged their use rather than central blocks whenever possible.^{1-3,6} It is of note that the majority of peripheral nerve blocks were truncal blocks: the ilioinguinal-iliohypogastric and the penile block. These two blocks were already the most frequently used truncal blocks in the ADARPEF study.² Similarly, to

what is reported in the present study, Polaner et al¹ noted that ilioinguinal-iliohypogastric blocks represented almost 40% of single-injection truncal blocks. Truncal blocks tend to replace caudal blocks for minor surgery in children, especially for lower abdominal surgery.^{7,8} This may reflect a change of anesthesia practice because of the efficiency and the safety of peripheral nerve blocks, when performed under ultrasound guidance.⁹ It is of note that penile blocks were performed without ultrasound guidance in more than 96% of the cases in the present study. The use of landmarks for the penile blocks may reflect the popularity of an easy to perform technique, supported by a recent study confirming the efficacy and long action of the penile block when compared to caudals.¹⁰ Moreover, recent studies demonstrated that the interest of ultrasound guidance for penile block in children is limited.^{11,12} Similar results were obtained with the pudendal nerve block, in comparison with caudal block, in terms of quality and duration of postoperative analgesia.¹³⁻¹⁵ Another potential explanation for the decrease in caudal blocks may be related to the recent concerns about the potential association between caudal anesthesia and the occurrence of urethral fistula following hypospadias repair.^{10,16,17}

Despite a wide variation in practice among the European countries (Table 2), the current analysis reveals that caudal blocks practice represents one third of RA in 2016 in Europe. There is a clear age-dependent practice with central blocks with caudals in particular being more frequently considered in children less than 3 years of age. Conversely, limb blocks were more frequently performed in children aged more than 3 years old. While the design of the current study does not allow a distinction between the different type of upper limb, lower limb, and craniofacial blocks, their practice was comparable to that reported earlier in the ADARPEF study² except for lower limb blocks which were reported in a higher percentage. Part of this difference could be due to different population recruitment and different surgical procedures being performed.

Ultrasound guidance is frequently utilized in the performance of pediatric regional anesthesia.^{9,18} Compared with other techniques ultrasound guidance is associated with an increased success rate, reduced onset time, moderately prolonged duration, and reduced need for local anesthetics.¹⁹ The value of ultrasound guidance was further demonstrated in young children.¹⁸ Despite these advantages, APRICOT study revealed that ultrasound guidance (associated or not with nerve stimulation) is only used in almost one third of truncal blocks, two third of upper and lower limb blocks, and very occasionally in central blocks. These findings are in contrast to those reported by PRAN where the use of ultrasound seems more obvious. These results are surprising and question on the reasons for not choosing this safe approach among European countries. One potential reason may be related to the low availability of ultrasound devices in some European countries (Table 3) and/or still lack of confidence among European anesthesiologists. Another cause of variability may be the lack of knowledge or teaching in some techniques in some European countries. Finally, the small sample in other countries also made it impossible to compare or conclude. Despite the fact that PRAN

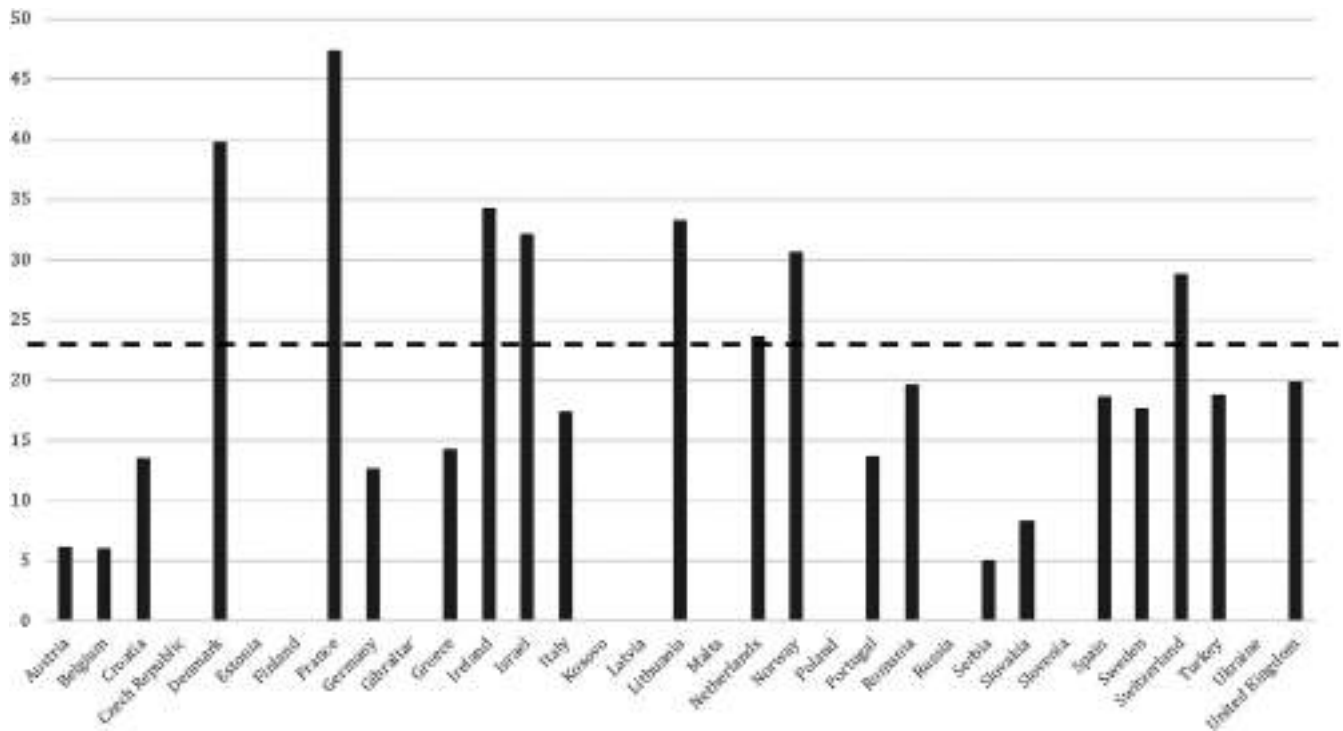


FIGURE 3 Percentage of ultrasound use for regional anesthesia (without others and infiltrations) per country (n = 4373). (Dashed line represents the percentage value of ultrasound use for regional anesthesia without others and infiltrations among all countries in Europe)

TABLE 3 Details of different blocks according to localizing aid techniques. Expressed in number (%) (The techniques of localizing aid missed in 4 patients in total)

Techniques	Landmarks	NS	US	US + NS	Total
Central blocks	1815 (97.4%)	3 (0.2)	41 (2.2%)	5 (0.3)	1864
Upper limb blocks	48 (18.5%)	41 (15.8%)	131 (50.6%)	39 (15.1%)	259
Lower limb blocks	47 (15.2%)	46 (14.9%)	140 (45.3%)	76 (24.6%)	309
Truncal blocks	1167 (63.8%)	65 (3.6%)	562 (30.7%)	36 (2%)	1830
Craniofacial	99 (89.2%)	1 (0.9%)	8 (7.2%)	3 (2.7%)	111
Total	3175 (72.6%)	156 (3.6%)	882 (20.2%)	159 (3.6%)	4373
Truncal					
II-IH blocks	263 (51.2%)	4 (0.8%)	234 (45.5%)	13 (2.5%)	514 (28.1%)
TAP blocks	10 (3.7%)	1 (0.4)	247 (90.1%)	16 (5.8%)	274 (15%)
Intercostal blocks	10 (76.9%)	0	3 (23.1%)	0	13 (0.7%)
Paraumbilical blocks	49 (46.7%)	0	56 (53.3%)	0	105 (5.7%)
Penile blocks	778 (97.4%)	0	21 (2.6%)	0	799 (43.6%)
Pudendal blocks	57 (45.6%)	60 (48%)	1 (0.8)	7 (5.6%)	125 (6.9%)
Total	1167 (63.8%)	65 (3.6%)	562 (30.7%)	36 (1.9%)	1830

Abbreviations: II-IH, ilioinguinal-iliohypogastric; TAP, trans-abdominis plane.

centers were self-referred and participation was subject to acceptance of the terms of the study, the nature of the PRAN register, which includes specific centers in the USA known for their ability to perform pediatric RA, may explain the difference observed with.^{1,3} Conversely, the APRICOT study was not focused on regional anesthesia and thus, the 261 selected European centers may not be all experts in RA.⁵

4.1 | Limitations

This study presents several potential limitations. APRICOT was designed to characterize the epidemiology of perioperative severe complications in Europe. However, it provided a snap shot of routine clinical practice, which was valuable to draw lessons and target teaching and education toward areas of improvement. On the

other hand, data concerning regional anesthesia were not detailed enough and information on the different types of upper or lower limbs block is missing as well as the doses of local anesthetics, and the distinction between single-injection block and continuous injection through a catheter. While no complications related to regional anesthesia were reported in APRICOT, it is important to note that study was not powered enough for this outcome. Unfortunately, the design of the initial study limited us to record only immediate complications (such as acute toxicity of regional anesthesia). Longer-term complications, such as prolonged motor block, paresthesia, and nerve damage, could not be identified. Nevertheless, using the Hanley formula,²⁰ we can estimate the upper limits of 95% confidence intervals for immediate complications in our study to 0.16% for both central (0/1865) and peripheral nerve blocks (0/2512). This incidence of potential complications is comparable to that reported earlier in the ADARPEF study.²

5 | CONCLUSION

APRICOT is the largest prospective cohort study performed in Europe concerning pediatric regional anesthesia. Even if this audit was not especially designed for it, APRICOT provided important information on clinical practice with no report of adverse events directly related to the regional anaesthesia. Furthermore, the results of the present study confirm the rate of RA use is comparable with the data from previous ADARPEF study. Ultrasound guidance was mainly used for peripheral nerve blocks while central blocks were performed using landmark techniques. Ropivacaine and levobupivacaine were the most often local anesthetics used in pediatric RA in the present study with clonidine as the adjuvant frequently used. Efforts should be made to increase the use of RA in European countries where regional analgesia practice is limited in order to improve postoperative pain management and decrease the use of systemic analgesic such as opioids.

CONFLICT OF INTEREST

Veyckemans F: Section editor in Paediatric Anesthesia. Habre W: Research grant received from Maquet (Getinge group, Solna, Sweden) in 2014 and not in relation with the current work. He acts currently as unpaid scientific consultant for Maquet (Getinge group, Solna, Sweden). The remaining authors have no conflict of interest.

ETHICAL APPROVAL

Ethics requirements differed among countries and even within a given country. Formal ethical approval or a waiver was applied for as appropriate in all participating centers. All details about ethical approvals can be obtained on the ESA website: <http://www.esahq.org/research/clinical-trial-network/ongoing-trials/apricot/documents>

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